```
=> fil cap
FILE 'CAPLUS' ENTERED AT 12:12:19 ON 20 FEB 2008
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FILE COVERS 1907 - 20 Feb 2008  VOL 148 ISS 8
FILE LAST UPDATED: 19 Feb 2008  (20080219/ED)

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They are available for your review at:

http://www.cas.org/infopolicy.html

=> d que l32
L1                STR
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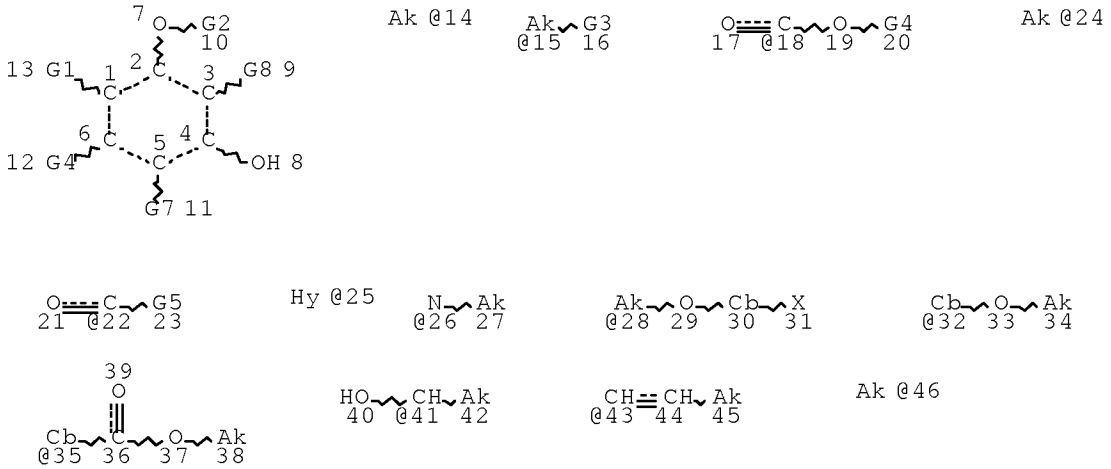


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VAR G2=H/14/15
VAR G3=18/22
VAR G4=H/24
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VAR G7=CHO/COOH
VAR G8=41/43/46
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CONNECT IS E2  RC AT  15
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  25
CONNECT IS E1  RC AT  27
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DEFAULT MLEVEL IS ATOM
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GGCAT   IS LIN  LOC  SAT  AT  15
GGCAT   IS LOC  AT  24
GGCAT   IS MCY  UNS  AT  25
GGCAT   IS LOC  AT  27
GGCAT   IS MCY  UNS  AT  30
GGCAT   IS MCY  UNS  AT  32
GGCAT   IS MCY  UNS  AT  35
GGCAT   IS SAT  AT  45
GGCAT   IS SAT  AT  46
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E5 C  E1 N  AT  25
ECOUNT  IS E6 C  AT  30
ECOUNT  IS E6 C  AT  32
ECOUNT  IS E6 C  AT  35
ECOUNT  IS M9 C  AT  46

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  46

STEREO ATTRIBUTES: NONE
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L30           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "BENZALDEHYDE, 3-CHLORO-6-HYD
                ROXY-4-METHOXY-2-METHYL-5-((2E,6E)-3-METHYL-7-((2S)-TETRAHYDRO-
                5,5-DIMETHYL-4-OXO-2-FURANYL)-2,6-OCTADIENYL)-"/CN
L31          21 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 OR L30
L32           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L31


=> d l32 ibib abs hitstr tot

L32  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2005:371202  CAPLUS  Full-text
DOCUMENT NUMBER:          142:430014
TITLE:                    Preparation of phenol derivatives as anti-trypanosoma
                          agents
INVENTOR(S):              Saimoto, Hiroyuki; Shigemasa, Yoshihiro; Kita,
                          Kiyoshi; Yabu, Yoshisada; Hosokawa, Tomoyoshi;
                          Yamamoto, Masaichi
PATENT ASSIGNEE(S):       Arigen, Inc., Japan
SOURCE:                   PCT Int. Appl., 40 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2005037759         A1    20050428    WO 2003-JP13310         20031017
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
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GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003273040	A1	20050505	AU 2003-273040	20031017
AU 2004282055	A1	20050428	AU 2004-282055	20041018
WO 2005037760	A1	20050428	WO 2004-JP15390	20041018

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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

EP 1681280	A1	20060719	EP 2004-792559	20041018

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IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

CN 1882523	A	20061220	CN 2004-80033945	20041018
IN 2006DN02774	A	20070803	IN 2006-DN2774	20060517
US 2007208078	A1	20070906	US 2006-575653	20061213

PRIORITY APPLN. INFO.:

WO 2003-JP13310	A	20031017
WO 2003-JP313310	A	20031017
WO 2004-JP15390	W	20041018

OTHER SOURCE(S): MARPAT 142:430014

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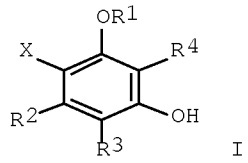


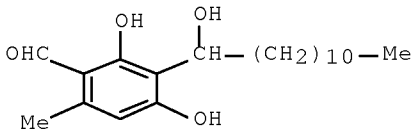
I

AB The title compds. I [X represents hydrogen or halogeno; R1 represents hydrogen, etc.; R2 represents hydrogen or C1-4 alkyl; R3 represents CHO or COOH; and R4 represents (CH2)mCH3 (wherein m is an integer of 1 to 14), etc.] are prepared Thus, 2,4-dihydroxy-3-(1-hydroxydodecyl)-6- methylbenzaldehyde was prepared from 2,4-dihydroxy-6-methylbenzaldehyde and dodecanal. Compds. of this invention in vitro showed IC50 values of 0.3 nM to 120 nM in an anti-trypanosoma assay.

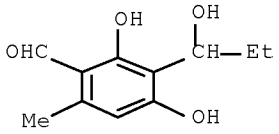
IT 850732-56-8P 850732-57-9P 850732-58-0P
850732-59-1P 850732-60-4P 850732-61-5P
850732-62-6P 850732-63-7P 850732-64-8P
850732-65-9P 850732-66-0P 850732-67-1P

850732-68-2P 850732-69-3P 850732-70-6P
850732-71-7P 850732-72-8P 850732-73-9P
850732-74-0P 850732-75-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenol derivs. as anti-trypanosoma agents)

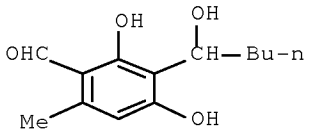
RN 850732-56-8 CAPLUS
CN Benzaldehyde, 2,4-dihydroxy-3-(1-hydroxydodecyl)-6-methyl- (CA INDEX NAME)



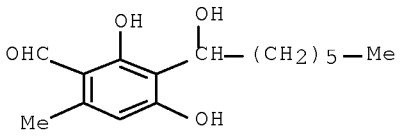
RN 850732-57-9 CAPLUS
CN Benzaldehyde, 2,4-dihydroxy-3-(1-hydroxypropyl)-6-methyl- (CA INDEX NAME)



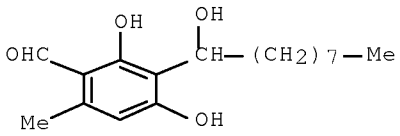
RN 850732-58-0 CAPLUS
CN Benzaldehyde, 2,4-dihydroxy-3-(1-hydroxypentyl)-6-methyl- (CA INDEX NAME)



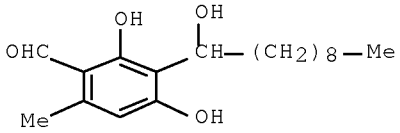
RN 850732-59-1 CAPLUS
CN Benzaldehyde, 2,4-dihydroxy-3-(1-hydroxyheptyl)-6-methyl- (CA INDEX NAME)



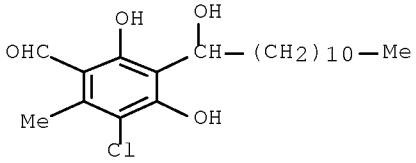
RN 850732-60-4 CAPLUS
CN Benzaldehyde, 2,4-dihydroxy-3-(1-hydroxynonyl)-6-methyl- (CA INDEX NAME)



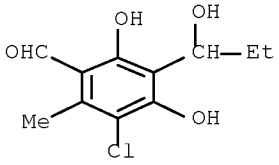
RN 850732-61-5 CAPLUS
CN Benzaldehyde, 2,4-dihydroxy-3-(1-hydroxydecyl)-6-methyl- (CA INDEX NAME)



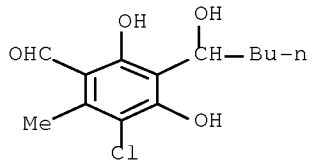
RN 850732-62-6 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-5-(1-hydroxydodecyl)-2-methyl- (CA INDEX NAME)



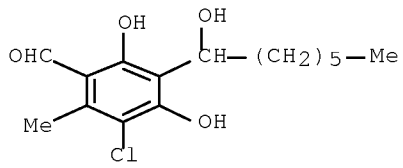
RN 850732-63-7 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-5-(1-hydroxypropyl)-2-methyl- (CA INDEX NAME)



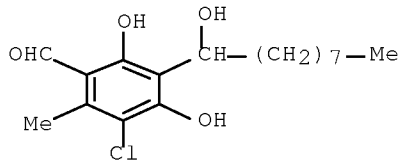
RN 850732-64-8 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-5-(1-hydroxypentyl)-2-methyl- (CA INDEX NAME)



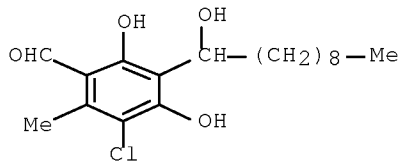
RN 850732-65-9 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-5-(1-hydroxyheptyl)-2-methyl- (CA INDEX NAME)



RN 850732-66-0 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-5-(1-hydroxynonyl)-2-methyl- (CA INDEX NAME)

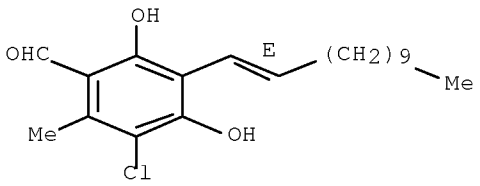


RN 850732-67-1 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-5-(1-hydroxydecyl)-2-methyl- (CA INDEX NAME)



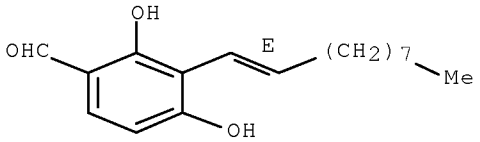
RN 850732-68-2 CAPLUS
CN Benzaldehyde, 3-chloro-5-(1E)-1-dodecenyl-4,6-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



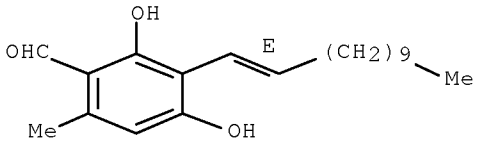
RN 850732-69-3 CAPLUS
CN Benzaldehyde, 3-(1E)-1-decenyl-2,4-dihydroxy- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



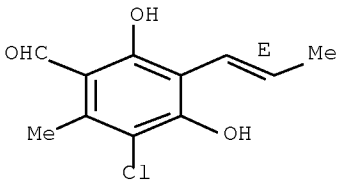
RN 850732-70-6 CAPLUS
CN Benzaldehyde, 3-(1E)-1-dodecenyl-2,4-dihydroxy-6-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



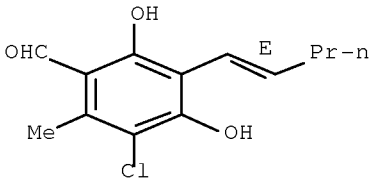
RN 850732-71-7 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-2-methyl-5-(1E)-1-propenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



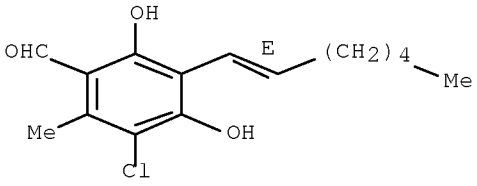
RN 850732-72-8 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-2-methyl-5-(1E)-1-pentenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



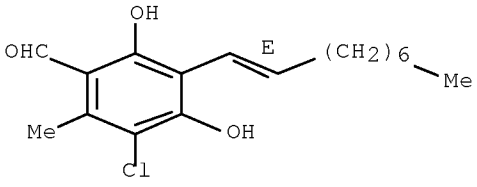
RN 850732-73-9 CAPLUS
CN Benzaldehyde, 3-chloro-5-(1E)-1-heptenyl-4,6-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



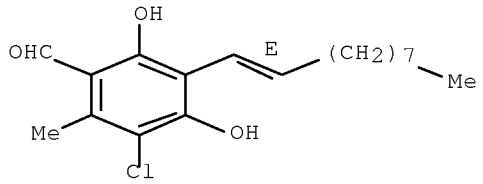
RN 850732-74-0 CAPLUS
CN Benzaldehyde, 3-chloro-4,6-dihydroxy-2-methyl-5-(1E)-1-nonenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 850732-75-1 CAPLUS
CN Benzaldehyde, 3-chloro-5-(1E)-1-decenyl-4,6-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:362051 CAPLUS Full-text
DOCUMENT NUMBER: 142:423803
TITLE: Prophylactic and therapeutic agents for cryptosporidiosis containing ascochlorins, ascofuranones, or dehydroascofuranones
INVENTOR(S): Kita, Kiyoshi; Yabu, Yoshisada; Nagai, Kazuo; Minagawa, Nobuko; Hosokawa, Tomoyoshi; Suzuki, Takashi; Ota, Nobuo
PATENT ASSIGNEE(S): Arigen, Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005112755	A	20050428	JP 2003-347395	20031006
PRIORITY APPLN. INFO.:			JP 2003-347395	20031006

OTHER SOURCE(S): MARPAT 142:423803
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

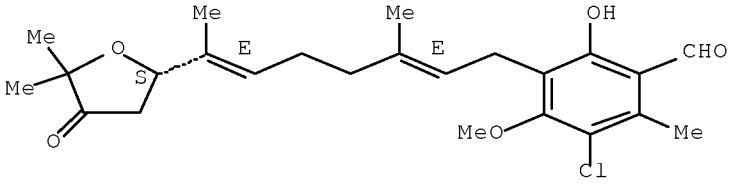
AB The agents contain ≥1 selected from ascochlorins I [R1 = CHO, CO2H; R2 = H, (CnH2n)R' (n = 1-5; R' = H, CO2R'' on any C atom of CnH2n; R'' = H, C1-3 alkyl), COR''' [R''' = pyridyl, c1-3 alkylamino, (halophenoxy)alkyl, C1-3 alkyl-Ph, (C1-3 alkoxycarbonyl)phenyl]], ascofuranones II , and dehydroascofuranones III, which inhibit cyanide-resistant quinol oxidase of Cryptosporidium. Thus, IC50 of ascofuranone against Cryptosporidium recombinant quinol oxidase was 0.3 nM. Tablets containing ascofuranone were also also formulated.
IT 611217-45-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prophylactic and therapeutic agents for cryptosporidiosis containing ascochlorins, ascofuranones, or dehydroascofuranones as cyanide-resistant quinol oxidase inhibitors)

RN 611217-45-9 CAPLUS

CN Benzaldehyde, 3-chloro-6-hydroxy-4-methoxy-2-methyl-5-[(2E,6E)-3-methyl-7-[(2S)-tetrahydro-5,5-dimethyl-4-oxo-2-furanyl]-2,6-octadienyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L32 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:643613 CAPLUS Full-text

DOCUMENT NUMBER: 139:307902

TITLE: Ascochlorin Derivatives as Ligands for Nuclear Hormone Receptors

AUTHOR(S): Togashi, Marie; Ozawa, Satoshi; Abe, Shoko; Nishimura, Tomoyuki; Tsuruga, Mie; Ando, Kunio; Tamura, Gakuzo; Kuwahara, Shigefumi; Ubukata, Makoto; Magae, Junji

CORPORATE SOURCE: Department of Biotechnology, Institute of Research and Innovation, Kashiwa, 277-0861, Japan

SOURCE: Journal of Medicinal Chemistry (2003), 46(19), 4113-4123
CODEN: JMCMAR; ISSN: 0022-2623

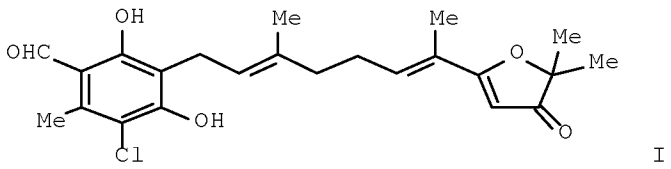
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:307902

GI



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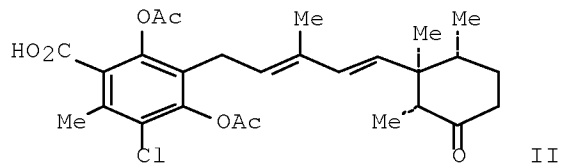


II

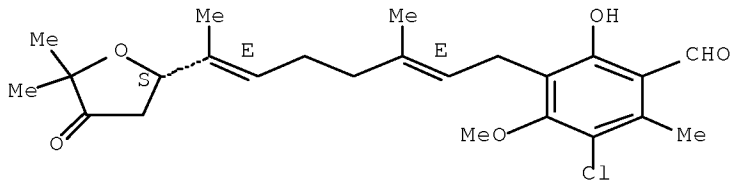
AB Nuclear receptor family proteins are structurally related transcription factors activated by specific lipophilic compds. Because they are activated by a variety of hormonal mols., including retinoic acid, vitamin D, and steroid hormones, they are assumed to be promising targets for clin. drugs. We previously found that one ascochlorin derivative, 4-O-carboxymethyl-ascochlorin, is a potent agonist of peroxisome proliferator activated receptor γ (PPARγ). Here, we synthesized derivs. of ascochlorin, designated as a lead compound, to create new modulators of nuclear hormone receptors. Two derivs., 4-O-carboxymethyl-2-O-methylascochlorin and 4-O-isonicotinoyl-2-O-methylascochlorin, showed improved agonistic activity for PPARγ and induced differentiation of a progenitor cell line, C3H10T1/2. We also found that ascochlorin, dehydroascofuranone (I), and an ascochlorin 2,4-O-diacetyl-1-carboxylic acid derivative (II) specifically activated estrogen receptors, PPARα, and an androgen receptor. All of the derivs. activated the pregnane X receptor. These results suggest that the chemical structure of ascochlorin is useful in designing novel modulators of nuclear receptors.

IT 611217-45-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of ascochlorin and ascofuranone derivs. as ligands for nuclear hormone receptors)

RN 611217-45-9 CAPLUS

CN Benzaldehyde, 3-chloro-6-hydroxy-4-methoxy-2-methyl-5-[(2E,6E)-3-methyl-7-[(2S)-tetrahydro-5,5-dimethyl-4-oxo-2-furanyl]-2,6-octadienyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 11:10:38 ON 20 FEB 2008)

FILE 'REGISTRY' ENTERED AT 11:10:44 ON 20 FEB 2008
L1 STR
L2 0 S L1
L3 20 S L1 FUL
L4 STR
L5 3 S L4
L6 46 S L4 FUL

FILE 'CAPLUS' ENTERED AT 11:39:00 ON 20 FEB 2008
L7 1 S L3
L8 96 S L6

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     FILE 'REGISTRY' ENTERED AT 11:39:18 ON 20 FEB 2008
L9             STR L4
L10             2 S L9 SAM SUB=L6
L11            32 S L9 FUL SUB=L6

     FILE 'CAPLUS' ENTERED AT 11:42:36 ON 20 FEB 2008
L12            93 S L11
L13           ANALYZE L12 1-93 RN :    1785 TERMS

     FILE 'REGISTRY' ENTERED AT 11:43:04 ON 20 FEB 2008
L14             1 S 38462-04-3
L15            31 S L11 NOT L14

     FILE 'CAPLUS' ENTERED AT 11:44:59 ON 20 FEB 2008
L16            34 S L15

     FILE 'REGISTRY' ENTERED AT 11:45:09 ON 20 FEB 2008
L17             0 S L15 AND C18H25CLO4/MF
L18             5 S L15 AND C=18
L19             2 S L18 AND H=25
L20             1 S L18 AND H=27
L21             0 S L11 AND C=21
L22            15 S L11 AND OC4/ES
L23            15 S L22 AND O=5
L24             0 S L23 AND N=1
L25             0 S H=23 AND L23
L26             3 S H=33 AND L23
L27             3 S H=31 AND L23
L28             0 S L26 AND C=23
L29             3 S L11 AND C=24
                  E BENZALDEHYDE, 3-CHLORO-6-HYDROXY-4-METHOXY-2-METHYL-5-((2E,6E
L30             1 S E3
L31            21 S L3 OR L30

     FILE 'CAPLUS' ENTERED AT 12:03:19 ON 20 FEB 2008
L32             3 S L31

     FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 12:05:30 ON 20 FEB 2008
                  E SAIMOTO H/AU
L33           206 S E3,E6-7
                  E SHIGEMASA Y/AU
L34           286 S E3,E5-6
                  E KITA K/AU
L35          1742 S E3-10,E80
                  E YOSHISADA Y/AU
                  E YABU Y/AU
L36            85 S E3-4,E12
                  E HOSOKAWA T/AU
L37          1970 S E81,E3-11
                  E YAMAMOTO M/AU
L38         17371 S E140,E3-75
L39         21463 S L33-38
L40           286 S L39 AND PHENOL
L41             0 S L40 AND ?PANASOM?
L42             0 S L40 AND (TRYPANASOM? OR ?PANASOM? OR ANTITRYPANA?)

     FILE 'CAPLUS' ENTERED AT 12:10:37 ON 20 FEB 2008
                  E US2006-575653/APPS
L43             1 S E3
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     FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 12:11:33 ON 20 FEB 2008
L44          46 S L39 AND (?PANOSOM? OR TRYPANOS? OR ANTITRYPANOS?)

     FILE 'CAPLUS' ENTERED AT 12:12:19 ON 20 FEB 2008

=> fil cap dissabs confsci wpix
FILE 'CAPLUS' ENTERED AT 12:13:05 ON 20 FEB 2008
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L33          206 SEA ("SAIMOTO H"/AU OR "SAIMOTO HIROYUKI"/AU OR "SAIMOTO
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L34          286 SEA ("SHIGEMASA Y"/AU OR "SHIGEMASA YOSHIHIRO"/AU OR "SHIGEMASA
                  YOSHIHRO"/AU)
L35         1742 SEA ("KITA K"/AU OR "KITA K A"/AU OR "KITA K F"/AU OR "KITA K
                 K F S P"/AU OR "KITA K M B"/AU OR "KITA K M C"/AU OR "KITA K N
                 G K K K K"/AU OR "KITA K S C"/AU OR "KITA KIYOSHI"/AU)
L36           85 SEA ("YABU Y"/AU OR "YABU Y T"/AU OR "YABU YOSHISADA"/AU)
L37         1970 SEA ("HOSOKAWA TOMOYOSHI"/AU OR "HOSOKAWA T"/AU OR "HOSOKAWA T
                 C O F"/AU OR "HOSOKAWA T D C"/AU OR "HOSOKAWA T F I C L"/AU OR
                 "HOSOKAWA T I G C L"/AU OR "HOSOKAWA T L"/AU OR "HOSOKAWA T N
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                 L"/AU OR "YAMAMOTO M S L"/AU OR "YAMAMOTO M S L O G L"/AU OR
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                OR "YAMAMOTO M T L T K"/AU OR "YAMAMOTO M Y"/AU OR "YAMAMOTO M
                Y F C L"/AU)
L39        21463 SEA (L33 OR L34 OR L35 OR L36 OR L37 OR L38)
L44           46 SEA L39 AND (?PANOSOM? OR TRYPANOS? OR ANTITRYPANOS?)


=> dup rem l44
PROCESSING COMPLETED FOR L44
L45           42 DUP REM L44 (4 DUPLICATES REMOVED)
                 ANSWERS '1-40' FROM FILE CAPLUS
                 ANSWER '41' FROM FILE CONFSCI
                 ANSWER '42' FROM FILE WPIX

=> d l45 ibib abs tot

L45  ANSWER 1 OF 42  CAPLUS  COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:469037  CAPLUS  Full-text
DOCUMENT NUMBER:          144:482220
TITLE:                    cDNA and protein sequences of Trypanosoma cruzi and
                          Leishmania major quinol oxidase and screening its
                          inhibitors for treatment of leishmaniasis and Chagas'
                          diseases
INVENTOR(S):              Suzuki, Takashi; Suzuki, Mitsuko; Yabu, Yoshisada;
                          Ota, Nobuo; Saimoto, Hiroyuki; Kita, Kiyoshi
PATENT ASSIGNEE(S):       Arigen, Inc., Japan
SOURCE:                   Jpn. Kokai Tokkyo Koho, 25 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     JP 2006122010         A     20060518    JP 2004-317308          20041029
PRIORITY APPLN. INFO.:                       JP 2004-317308          20041029
AB    This invention provides cDNA and protein sequences of quinol oxidase from
      Trypanosoma cruzi and Leishmania major.  This invention also provides
      Leishmania major quinol oxidase without cross reacting with AOX, a quinol
      oxidase from T. brucei.  The enzyme activity of quinol oxidase was inhibited
      by ascofuranone and, the ascofuranone also inhibited the growth of Trypanosoma
      cruzi.  Combining with cytochrome respiratory chain inhibitor, the inhibitors
      of quinol oxidase can be used for treatment of leishmaniasis and Chagas'
      diseases caused by infection of Trypanosoma cruzi and Leishmania major.


L45  ANSWER 2 OF 42  CAPLUS  COPYRIGHT 2008 ACS on STN DUPLICATE 2
ACCESSION NUMBER:         2005:371202  CAPLUS  Full-text
DOCUMENT NUMBER:          142:430014
TITLE:                    Preparation of phenol derivatives as
                          anti-trypanosoma agents
INVENTOR(S):              Saimoto, Hiroyuki; Shigemasa, Yoshihiro; Kita,
                          Kiyoshi; Yabu, Yoshisada; Hosokawa, Tomoyoshi;
                          Yamamoto, Masaichi
PATENT ASSIGNEE(S):       Arigen, Inc., Japan
SOURCE:                   PCT Int. Appl., 40 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
```

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037759	A1	20050428	WO 2003-JP13310	20031017
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003273040	A1	20050505	AU 2003-273040	20031017
AU 2004282055	A1	20050428	AU 2004-282055	20041018
WO 2005037760	A1	20050428	WO 2004-JP15390	20041018
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1681280	A1	20060719	EP 2004-792559	20041018
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CN 1882523	A	20061220	CN 2004-80033945	20041018
IN 2006DN02774	A	20070803	IN 2006-DN2774	20060517
US 2007208078	A1	20070906	US 2006-575653	20061213

PRIORITY APPLN. INFO.:	WO 2003-JP13310	A	20031017
	WO 2003-JP313310	A	20031017
	WO 2004-JP15390	W	20041018

OTHER SOURCE(S): MARPAT 142:430014
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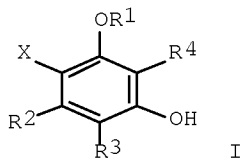

I

AB The title compds. I [X represents hydrogen or halogeno; R1 represents hydrogen, etc.; R2 represents hydrogen or C1-4 alkyl; R3 represents CHO or COOH; and R4 represents (CH2)mCH3 (wherein m is an integer of 1 to 14), etc.] are prepared Thus, 2,4-dihydroxy-3-(1-hydroxydodecyl)-6- methylbenzaldehyde

was prepared from 2,4-dihydroxy-6-methylbenzaldehyde and dodecanal. Compds. of this invention in vitro showed IC50 values of 0.3 nM to 120 nM in an anti-trypanosoma assay.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:677762 CAPLUS Full-text
DOCUMENT NUMBER: 141:167741
TITLE: Indole alkaloids as enhancers for antiprotozoal activity of ascofuranone, their compositions and kits, and treatment of protozoan diseases with them
INVENTOR(S): Kita, Kiyoshi; Yabu, Yoshisada; Nagai, Kazuo; Minagawa, Nobuko; Hosokawa, Kazuyoshi
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004231601	A	20040819	JP 2003-24643	20030131

PRIORITY APPLN. INFO.: JP 2003-24643 20030131
AB Title enhancers, useful for treatment of African trypanosoma, etc., contain indole alkaloids, e.g. in Picrasma quassioides. Thus, benzalharman at 25 μM inhibited glycerokinase by 62.1%. Benzalharman enhanced the antiprotozoal activity of ascofuranone with ED50 of 8.5 μM.

L45 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1997:453440 CAPLUS Full-text
DOCUMENT NUMBER: 127:156717
TITLE: Protozoacides containing isoprenoid antibiotics, ascochlorin, ascofuranone, or their derivatives
INVENTOR(S): Minagawa, Nobuko; Yabu, Yoshisada; Kita, Kiyoshi; Nagai, Kazuo; Hosokawa, Tomoyoshi
PATENT ASSIGNEE(S): Hosokawa, Tomoyoshi, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09165332	A	19970624	JP 1995-351093	19951215

PRIORITY APPLN. INFO.: JP 1995-351093 19951215
OTHER SOURCE(S): MARPAT 127:156717
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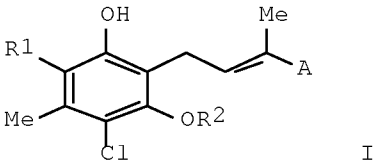

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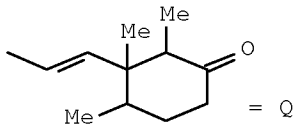

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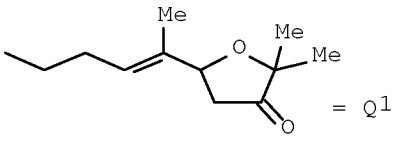

= Q1

AB The protozoacides contain ascochlorins I [A = Q; R1 = CHO, CO2H; R2 = (CnH2n)R3 (n = 1-5; R3 = H, CO2R4; R4 = H, C1-3 alkyl), COR5 (R5 = pyridyl, C1-3 alkylamino, halophenoxyalkyl, Ph substituted with C1-3 alkoxy or C1-3 alkoxycarbonyl)] or ascofuranones I (A = Q1) as active ingredients. The protozoacides are useful for prevention and treatment of African trypanosomiasis and trypanosomiasis of domestic animals. Ascochlorin inhibited in vitro growth of circulating-form Trypanosoma brucei brucei in the presence of glycerin. .

L45 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1003374 CAPLUS Full-text
TITLE: Trypanosoma brucei vacuolar protein sorting 41 (VPS41) is required for intracellular iron utilization and maintenance of normal cellular morphology
AUTHOR(S): Lu, S.; Suzuki, T.; Iizuka, N.; Ohshima, S.; Yabu, Y.; Suzuki, M.; Wen, L.; Ohta, N.
CORPORATE SOURCE: Department of Molecular Parasitology, Graduate School of Medical Sciences, Nagoya City University, Nagoya, 467-8601, Japan
SOURCE: Parasitology (2007), 134(11), 1639-1647
CODEN: PARAAE; ISSN: 0031-1820
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Procyclic forms of Trypanosoma brucei brucei remain and propagate in the midgut of tsetse fly where iron is rich. Addnl. iron is also required for their growth in in vitro culture. However, little is known about the genes involved in iron metabolism and the mechanism of iron utilization in procyclic-form cells. Therefore, we surveyed the genes involved in iron metabolism in the T. b. brucei genome sequence database. We found a potential homolog of vacuole protein sorting 41 (VPS41), a gene that is required for high-affinity iron transport in Saccharomyces cerevisiae and cloned the full-length gene (TbVPS41). Complementation anal. of TbVPS41 in ΔScvps41 yeast cells showed that TbVPS41 could partially suppress the inability of ΔScvps41 yeast cells to grow on low-iron medium, but it could not suppress the fragmented vacuole phenotype. Further RNA interference (RNAi)-mediated gene knock-down in procyclic-form cells resulted in a significant reduction of growth in low-iron medium; however, no change in growth was observed in normal culture medium. Transmission electron microscopy showed that RNAi caused T. b. brucei cells to have larger nos. of small intracellular vesicles, similar to the fragmented vacuoles observed in ΔScvps41 yeast cells. The present study demonstrates that TbVPS41 plays an important role in the intracellular

iron utilization system as well as in the maintenance of normal cellular morphol.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:476913 CAPLUS Full-text
DOCUMENT NUMBER: 147:249690
TITLE: Advances in drug discovery and biochemical studies
AUTHOR(S): Kita, Kiyoshi; Shiomi, Kazuro; Omura, Satoshi
CORPORATE SOURCE: Department of Biomedical Chemistry, Graduate School of Medicine, University of Tokyo, Tokyo, 113-0033, Japan
SOURCE: Trends in Parasitology (2007), 23(5), 223-229
CODEN: TPRACT; ISSN: 1471-4922
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Japanese researchers continue to discover new means to combat parasites and make important contributions toward developing tools for global control of parasitic diseases. Streptomyces avermectinius, the source of ivermectin, was discovered in Japan in the early 1970s and renewed and vigorous screening of microbial metabolites in recent years has led to the discovery of new antiprotozoals and anthelmintics, including antimalarial drugs. Intensive studies of parasite energy metabolism, such as NADH-fumarate reductase systems and the synthetic pathways of nucleic acids and amino acids, also contribute to the identification of novel and unique drug targets.
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:58924 CAPLUS Full-text
DOCUMENT NUMBER: 145:39855
TITLE: Chemotherapeutic efficacy of ascofuranone in Trypanosoma vivax-infected mice without glycerol
AUTHOR(S): Yabu, Yoshisada; Suzuki, Takashi; Nihei, Coh-ichi; Minagawa, Nobuko; Hosokawa, Tomoyoshi; Nagai, Kazuo; Kita, Kiyoshi; Ohta, Nobuo
CORPORATE SOURCE: Department of Molecular Parasitology, Graduate School of Medical Sciences, Nagoya City University, Nagoya, 467-8601, Japan
SOURCE: Parasitology International (2006), 55(1), 39-43
CODEN: PAINFD; ISSN: 1383-5769
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ascofuranone, an antibiotic isolated from Ascochyta visiae, showed trypanocidal activity in Trypanosoma vivax-infected mice. A single dose of 50 mg/kg ascofuranone effectively cured the mice without the help of glycerol. Repeated administrations of this drug further enhanced its chemotherapeutic effect. After two, three, and four consecutive days treatment, the doses needed to cure the infection decreased to 25, 12, and 6 mg/kg, so that the total doses administered were 50, 36 and 24 mg/kg, resp. Ascofuranone (50 mg/kg) also had a prophylactic effect against T. vivax infection within the first two days after administration. This prophylactic activity diminished to 80% by day 3 and completely disappeared four days after administration. Of particular interest in this study was that ascofuranone had trypanocidal activity in T. vivax-infected mice in the absence of glycerol, whereas co-administration of glycerol or repeated administrations of this drug are needed for Trypanosoma brucei brucei infection. Our present results strongly suggest

that ascofuranone is also an effective tool in chemotherapy against African trypanosomiasis in domestic animals.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:58922 CAPLUS Full-text
DOCUMENT NUMBER: 145:285774
TITLE: Genetic diversity and kinetic properties of Trypanosoma cruzi dihydroorotate dehydrogenase isoforms
AUTHOR(S): Sariego, Idalia; Annoura, Takeshi; Nara, Takeshi; Hashimoto, Muneaki; Tsubouchi, Akiko; Iizumi, Kyoichi; Makiuchi, Takashi; Murata, Eri; Kita, Kiyoshi; Aoki, Takashi
CORPORATE SOURCE: Department of Molecular and Cellular Parasitology, Juntendo University School of Medicine, Hongo 2-1-1, Bunkyo-ku, Tokyo, 113-8421, Japan
SOURCE: Parasitology International (2006), 55(1), 11-16
CODEN: PAINFD; ISSN: 1383-5769
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dihydroorotate dehydrogenase (DHOD) is the fourth enzyme in the de novo pyrimidine biosynthetic pathway and is essential in Trypanosoma cruzi, the parasitic protist causing Chagas' disease. T. cruzi and human DHOD have different biochem. properties, including the electron acceptor capacities and cellular localization, suggesting that T. cruzi DHOD may be a potential chemotherapeutic target against Chagas' disease. Here, we report nucleotide sequence polymorphisms of T. cruzi DHOD genes and the kinetic properties of the recombinant enzymes. T. cruzi Tulahuen strain possesses three DHOD genes: DHOD1 and DHOD2, involved in the pyrimidine biosynthetic (pyr) gene cluster on an 800 and a 1000 kb chromosomal DNA, resp., and DHOD3, located on an 800 kb DNA. The open reading frames of all three DHOD genes are comprised of 942 bp, and encode proteins of 314 amino acids. The three DHOD genes differ by 26 nucleotides, resulting in replacement of 8 amino acid residues. In contrast, all residues critical for constituting the active site are conserved among the three proteins. Recombinant T. cruzi DHOD1 and DHOD2 expressed in E. coli possess similar enzymic properties, including optimal pH, optimal temperature, Vmax, and Km for dihydroorotate and fumarate. In contrast, DHOD3 had a higher Vmax and Km for both substrates. Orotate competitively inhibited all three DHOD enzymes to a comparable level. These results suggest that, despite their genetic variations, kinetic properties of the three T. cruzi DHODs are conserved. Our findings facilitate further exploitation of T. cruzi DHOD inhibitors, as chemotherapeutic agents against Chagas' disease.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1227142 CAPLUS Full-text
DOCUMENT NUMBER: 144:48333
TITLE: mtDNA of parasites
AUTHOR(S): Watanabe, Yoh-ichi; Kita, Kiyoshi
CORPORATE SOURCE: Grad. Sch. Med., The Univ. Tokyo, Japan
SOURCE: Tanpakushitsu Kakusan Koso (2005), 50(14, Zokan), 1817-1821
CODEN: TAKKAJ; ISSN: 0039-9450
PUBLISHER: Kyoritsu Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on mtDNA, codon, functional RNA, mitochondrial protein synthesis, RNA editing, etc., in helminth, trypanosoma, and Plasmodium falciparum.

L45 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1062216 CAPLUS Full-text
DOCUMENT NUMBER: 144:288361
TITLE: Expression, purification and crystallization of Trypanosoma cruzi dihydroorotate dehydrogenase complexed with orotate
AUTHOR(S): Inaoka, Daniel Ken; Takashima, Eizo; Osanai, Arihiro; Shimizu, Hironari; Nara, Takeshi; Aoki, Takashi; Harada, Shigeharu; Kita, Kiyoshi
CORPORATE SOURCE: Department of Biomedical Chemistry, Graduate School of Medicine, University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Acta Crystallographica, Section F: Structural Biology and Crystallization Communications (2005), F61(10), 875-878
CODEN: ACSFCL; ISSN: 1744-3091
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Dihydroorotate dehydrogenase (DHOD) catalyzes the oxidation of dihydroorotate to orotate, the 4th step and the only redox reaction in the de novo biosynthesis of pyrimidine. Here, DHOD of T. cruzi (TcDHOD) was expressed as a recombinant protein in Escherichia coli and purified to homogeneity. Crystals of the TcDHOD-orotate complex were grown at 277 K by the sitting-drop vapor-diffusion technique using polyethylene glycol 3350 as precipitant. The crystals diffracted to better than 1.8 Å resolution using synchrotron radiation (λ = 0.900 Å). X-ray diffraction data were collected at 100 K and processed to 1.9 Å resolution with 98.2% completeness and an overall Rmerge of 7.8%. The TcDHOD crystals belonged to orthorhombic space group P212121, with unit-cell parameters a = 67.87, b = 71.89, and c = 123.27 Å. The presence of 2 mols. in the asym. unit (2 × 34 kDa) gave a crystal volume per protein weight (VM) of 2.2 Å3 Da-1 and a solvent content of 44%.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:647389 CAPLUS Full-text
DOCUMENT NUMBER: 143:244041
TITLE: Mutational analysis of the Trypanosoma vivax alternative oxidase: The E(X)6Y motif is conserved in both mitochondrial alternative oxidase and plastid terminal oxidase and is indispensable for enzyme activity
AUTHOR(S): Nakamura, Kosuke; Sakamoto, Kimitoshi; Kido, Yasutoshi; Fujimoto, Yoko; Suzuki, Takashi; Suzuki, Mitsuko; Yabu, Yoshisada; Ohta, Nobuo; Tsuda, Akiko; Onuma, Misao; Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medicine, Department of Biomedical Chemistry, The University of Tokyo, Tokyo, 113-0033, Japan
SOURCE: Biochemical and Biophysical Research Communications (2005), 334(2), 593-600
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Based on amino acid sequence similarity and the ability to catalyze the four-electron reduction of oxygen to water using a quinol substrate, mitochondrial alternative oxidase (AOX) and plastid terminal oxidase (PTOX) appear to be two closely related members of the membrane-bound diiron carboxylate group of proteins. In the current studies, we took advantage of the high activity of Trypanosoma vivax AOX (TvAOX) to examine the importance of the conserved Glu and the Tyr residues around the predicted third helix region of AOXs and PTOXs. We first compared the amino acid sequences of TvAOX with AOXs and PTOXs from various taxa and then performed alanine-scanning mutagenesis of TvAOX between amino acids Y199 and Y247. We found that the ubiquinol oxidase activity of TvAOX is completely lost in the E214A mutant, whereas mutants E215A and E216A retained more than 30% of the wild-type activity. Among the Tyr mutants, a complete loss of activity was also observed for the Y221A mutant, whereas the activities were equivalent to wild-type for the Y199A, Y212A, and Y247A mutants. Finally, residues Glu214 and Tyr221 were found to be strictly conserved among AOXs and PTOXs. Based on these findings, it appears that AOXs and PTOXs are a novel subclass of diiron carboxylate proteins that require the conserved motif E(X)6Y for enzyme activity.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:993083 CAPLUS Full-text

DOCUMENT NUMBER: 144:287178

TITLE: Alternative oxidase (AOX) genes of African trypanosomes: phylogeny and evolution of AOX and plastid terminal oxidase families

AUTHOR(S): Suzuki, Takashi; Hashimoto, Tetsuo; Yabu, Yoshisada; Majiwa, Phelix A. O.; Ohshima, Shigeru; Suzuki, Mitsuko; Lu, Shaohong; Hato, Mariko; Kido, Yasutoshi; Sakamoto, Kimitoshi; Nakamura, Kosuke; Kita, Kiyoshi; Ohta, Nobuo

CORPORATE SOURCE: Department of Molecular Parasitology, Graduate School of Medical Sciences, Nagoya City University, Kawasumi, Mizuho, Nagoya, 467-8601, Japan

SOURCE: Journal of Eukaryotic Microbiology (2005), 52(4), 374-381
CODEN: JEMIED; ISSN: 1066-5234

PUBLISHER: Blackwell Publishing, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To clarify evolution and phylogenetic relationships of trypanosome alternative oxidase (AOX) mols., AOX genes (cDNAs) of the African trypanosomes, Trypanosoma congolense and Trypanosoma evansi, were cloned by PCR. Both AOXs possess conserved consensus motifs (-E-, -EXXH-). The putative amino acid sequence of the AOX of T. evansi was exactly the same as that of T. brucei. A protein phylogeny of trypanosome AOXs revealed that three genetically and pathogenically distinct strains of T. congolense are closely related to each other. When all known AOX sequences collected from current databases were analyzed, the common ancestor of these three Trypanosoma species shared a sister-group position to T. brucei/T. evansi. Monophyly of Trypanosoma spp. was clearly supported (100% bootstrap value) with Trypanosoma vivax placed at the most basal position of the Trypanosoma clade. Monophyly of other eukaryotic lineages, terrestrial plants + red algae, Metazoa, diatoms, Alveolata, oomycetes, green algae, and Fungi, was reconstructed in the best AOX tree obtained from maximum likelihood anal., although some of these clades were not strongly supported. The terrestrial plants + red algae clade showed the closest affinity with an α-proteobacterium. Novosphingobium aromaticivorans, and the common ancestor of these lineages, was separated from

other eukaryotes. Although the root of the AOX subtree was not clearly determined, subsequent phylogenetic anal. of the composite tree for AOX and plastid terminal oxidase (PTOX) demonstrated that PTOX and related cyanobacterial sequences are of a monophyletic origin and their common ancestor is linked to AOX sequences.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:8554 CAPLUS Full-text
DOCUMENT NUMBER: 140:232201
TITLE: Direct evidence for cyanide-insensitive quinol oxidase (alternative oxidase) in apicomplexan parasite Cryptosporidium parvum: phylogenetic and therapeutic implications
AUTHOR(S): Suzuki, Takashi; Hashimoto, Tetsuo; Yabu, Yoshisada; Kido, Yasutoshi; Sakamoto, Kimitoshi; Nihei, Coh-ichi; Hato, Mariko; Suzuki, Shu-ichi; Amano, Yuko; Nagai, Kazuo; Rosokawa, Tomoyoshi; Minagawa, Nobuko; Ohta, Nobuo; Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medical Sciences, Department of Molecular Parasitology, Nagoya City University, Nagoya, 467-8601, Japan
SOURCE: Biochemical and Biophysical Research Communications (2004), 313(4), 1044-1052
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cryptosporidium parvum is a parasitic protozoan that causes the diarrheal disease cryptosporidiosis, for which no satisfactory chemotherapy is currently available. Although the presence of mitochondria in this parasite has been suggested, its respiratory system is poorly understood due to difficulties in performing biochem. analyses. In order to better understand the respiratory chain of C. parvum, we surveyed its genomic DNA database in GenBank and identified a partial sequence encoding cyanide-insensitive alternative oxidase (AOX). Based on this sequence, we cloned C. parvum AOX (CpAOX) cDNA from the phylum Apicomplexa for the first time. The deduced amino acid sequence (335 a.a.) of CpAOX contains diiron coordination motifs (-E-, -EXXH-) that are conserved among AOXs. Phylogenetic anal. suggested that CpAOX is a mitochondrial-type AOX, possibly derived from mitochondrial endosymbiont gene transfer. The recombinant enzyme expressed in Escherichia coli showed quinol oxidase activity. This activity was insensitive to cyanide and highly sensitive to ascofuranone, a specific inhibitor of trypanosome AOX.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:885782 CAPLUS Full-text
DOCUMENT NUMBER: 141:374297
TITLE: Drug development at global level
AUTHOR(S): Kita, Kiyoshi
CORPORATE SOURCE: Grad. Sch. Med., The Univ. Tokyo, Japan
SOURCE: Farumashia (2004), 40(10), 909-913
CODEN: FARUAW; ISSN: 0014-8601
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on the development of parasiticides, especially, ascofuranone, which inhibits trypanosome alternative oxidase for control of Trypanosoma brucei in treatment of African trypanosomiasis.

L45 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:404924 CAPLUS Full-text
DOCUMENT NUMBER: 141:200963
TITLE: Molecular cloning and characterization of Trypanosoma vivax alternative oxidase (AOX) gene, a target of the trypanocide ascofuranone
AUTHOR(S): Suzuki, Takashi; Nihei, Coh-Ichi; Yabu, Yoshisada; Hashimoto, Tetsuo; Suzuki, Mitsuko; Yoshida, Ayako; Nagai, Kazuo; Hosokawa, Tomoyoshi; Minagawa, Nobuko; Suzuki, Shuichi; Kita, Kiyoshi; Ohta, Nobuo
CORPORATE SOURCE: Graduate School of Medical Sciences, Department of Molecular Parasitology, Nagoya City University, Nagoya, 467-8601, Japan
SOURCE: Parasitology International (2004), 53(3), 235-245
CODEN: PAINFD; ISSN: 1383-5769
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trypanosoma vivax causes nagana disease in cattle. Since T. vivax is transmitted not only by tsetse flies but also by other biting flies (non-cyclic transmission), the parasite has been distributed to and has had a significant economic impact on wide geog. areas, including Africa and South America. Our previous study on Trypanosoma brucei brucei showed that the trypanosome alternative oxidase (TAO, TbAOX) is a promising target of chemotherapy. For this reason, we also have cloned the T. vivax AOX (TvAOX) gene and characterized the recombinant enzyme. The deduced amino acid sequence (328 a.a.) of TvAOX shares 76% identity with TbAOX and contains the diiron-coordination motifs (-E-, -EXXH-) that are conserved among AOXs. The Km of recombinant TvAOX (rTvAOX) expressed in Escherichia coli for ubiquinol (87.0±0.54 μM) was significantly lower than the value for recombinant TbAOX (rTbAOX) (714±4.5 μM). Ascofuranone, the most potent inhibitor of TbAOX, was a competitive inhibitor of rTvAOX with a Ki value (0.40±0.00 nM) significantly lower than that for rTbAOX (1.29±0.00 nM). The non-cyclic transmission ability of T. vivax and the in vivo chemotherapeutic efficacy of ascofuranone against T. vivax and T. b. brucei infection are discussed in terms of these Km and Ki values.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:926536 CAPLUS Full-text
DOCUMENT NUMBER: 140:209735
TITLE: Parasite mitochondria as drug target: Diversity and dynamic changes during the life cycle
AUTHOR(S): Kita, Kiyoshi; Nihei, Coichi; Tomitsuka, Eriko
CORPORATE SOURCE: Department of Biomedical Chemistry, Graduate School of Medicine, University of Tokyo, Tokyo, 113-0033, Japan
SOURCE: Current Medicinal Chemistry (2003), 10(23), 2535-2548
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Parasites have developed a wide variety of physiol. functions to survive within the specialized environments of the host. Regarding energy

metabolism, which represents an essential factor for survival, parasites adapt low oxygen tension in host mammals using metabolic systems that differ substantially from those of the host. Most parasites do not use free oxygen available within the host, but employ systems other than oxidative phosphorylation for ATP synthesis. Furthermore, parasites display marked changes in mitochondrial morphol. and components during the life cycle, and these represent very interesting elements of biol. processes such as developmental control and environmental adaptation. The enzymes in parasite-specific pathways offer potential targets for chemotherapy. Cyanide-insensitive trypanosome alternative oxidase (TAO) is the terminal oxidase of the respiratory chain of long slender bloodstream forms of the African trypanosome, which causes sleeping sickness. Recently, the most potent inhibitor of TAO to date, ascofuranone, was isolated from the phytopathogenic fungus, Ascochyta visiae. The inhibitory mechanisms of ascofuranone have been revealed using recombinant enzyme. Parasite-specific respiratory systems are also found in helminths. The NADH-fumarate reductase system in mitochondria form a final step in the phosphoenolpyruvate carboxykinase (PEPCK)-succinate pathway, which plays an important role in anaerobic energy metabolism for the Ascaris suum adult. Enzymes in this system, such as NADH-rhodoquinone reductase (complex I) and rhodoquinol-fumarate reductase (complex II), form promising targets for chemotherapy. In fact, a specific inhibitor of nematode complex I, nafuredin, has been found in mass-screening using parasite mitochondria.

REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:822795 CAPLUS Full-text
DOCUMENT NUMBER: 139:357611
TITLE: Ascofuranone as a chemotherapeutic agent of African sleeping sickness
AUTHOR(S): Yabu, Yoshisada; Suzuki, Takashi; Kita, Kiyoshi
CORPORATE SOURCE: Dep. Mol. Parasitol., Nagoya City Univ., Nagoya, 467-8601, Japan
SOURCE: Baiosaiensu to Indasutori (2003), 61(10), 681-682
CODEN: BIDSE6; ISSN: 0914-8981
PUBLISHER: Baioindasutori Kyokai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on African sleeping sickness caused by Trypanosoma infection, inhibition of trypanosome alternative oxidase by ascofuranone, and therapeutic effect of ascofuranone in African sleeping sickness mouse models.

L45 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:621706 CAPLUS Full-text
DOCUMENT NUMBER: 139:335515
TITLE: Metabolic characteristics in parasites
AUTHOR(S): Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medicine, University of Tokyo, Japan
SOURCE: Chiryogaku (2003), 37(6), 592-596
CODEN: CHRYDT; ISSN: 0386-8109
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, on energy metabolism and related enzymes in parasites, discussing the metabolism of nucleic acids, amino acids, and lipids in parasites, such as Ascaris suum, and Trypanosoma cruzi.

L45 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:787439 CAPLUS Full-text
DOCUMENT NUMBER: 140:180196
TITLE: Overproduction of highly active trypanosome alternative oxidase in Escherichia coli heme-deficient mutant
AUTHOR(S): Fukai, Yoshihisa; Nihei, Coichi; Kawai, Keisuke; Yabu, Yoshisada; Suzuki, Takasi; Ohta, Nobuo; Minagawa, Nobuko; Nagai, Kazuo; Kita, Kiyoshi
CORPORATE SOURCE: Department of Biomedical Chemistry, Graduate School of Medicine, University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Parasitology International (2003), 52(3), 237-241
CODEN: PAINFD; ISSN: 1383-5769
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyanide-insensitive trypanosome alternative oxidase (TAO) is the terminal oxidase of the respiratory chain of long slender bloodstream forms of the African trypanosome, which causes sleeping sickness in humans and nagana in cattle. TAO has been targeted for the development of anti-trypanosomal drugs, because it does not exist in the host. In this study, we established a system for overprodn. of highly active TAO in Escherichia coli heme-deficient mutant. Kinetic anal. of recombinant enzyme and TAO in Trypanosoma brucei brucei mitochondria revealed that recombinant TAO retains the properties of native enzyme, indicating that recombinant TAO is quite valuable for further biochem. study of TAO.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:443379 CAPLUS Full-text
DOCUMENT NUMBER: 140:22662
TITLE: The efficacy of ascofuranone in a consecutive treatment on Trypanosoma brucei brucei in mice
AUTHOR(S): Yabu, Yoshisada; Yoshida, Ayako; Suzuki, Takashi; Nihei, Coh-ichi; Kawai, Keisuke; Minagawa, Nobuko; Hosokawa, Tomoyoshi; Nagai, Kazuo; Kita, Kiyoshi; Ohta, Nobuo
CORPORATE SOURCE: Department of Molecular Parasitology, Nagoya City University, Nagoya, 467-8601, Japan
SOURCE: Parasitology International (2003), 52(2), 155-164
CODEN: PAINFD; ISSN: 1383-5769
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Consecutive administration of ascofuranone without glycerol was found to have therapeutic efficacy against Trypanosoma brucei brucei infection in mice. A suspension of ascofuranone (25-100 mg/kg) was administered i.p. every 24 h for 1-4 consecutive days to trypanosome-infected mice and efficacy was compared with oral treatment. With i.p. administration, all mice treated with 100 mg/kg ascofuranone for 4 consecutive days were cured. On contrary, with oral treatment a higher dose of ascofuranone (400 mg/kg) was needed for 8 consecutive days to cure the mice. With i.p. treatment, parasitemia was strongly suppressed, with almost all long slender bloodstream forms of the parasite changed to short stumpy forms by day 3 and the parasites were eliminated 4 days after the start of treatment. These ascofuranone-induced short stumpy forms were morphol. analogous to the stumpy forms 2 days after

peak parasitemia of pleomorphic clone of T. b. brucei GUTat 3.1. However, the properties of ubiquinol oxidase activity, which is the target of ascofuranone, in mitochondria isolated from before and after treatment, were almost same. The enzymic activities of ubiquinol oxidase were only decreased to approx. 30% within a day after treatment, and then kept at nearly the same level. In the present study, we have improved the regimen for administration of ascofuranone without glycerol, and demonstrated that consecutively administered ascofuranone showed trypanocidal effects in T. b. brucei infected mice. Our present results strongly suggest that consecutive administration of ascofuranone may be an effective chemotherapy for African trypanosomiasis.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:196106 CAPLUS Full-text
DOCUMENT NUMBER: 139:32393
TITLE: Purification of active recombinant trypanosome alternative oxidase
AUTHOR(S): Nihei, Coichi; Fukai, Yoshihisa; Kawai, Keisuke; Osanai, Arihiro; Yabu, Yoshisada; Suzuki, Takashi; Ohta, Nobuo; Minagawa, Nobuko; Nagai, Kazuo; Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medicine, Department of Biomedical Chemistry, University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: FEBS Letters (2003), 538(1-3), 35-40
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trypanosome alternative oxidase (TAO) is the terminal oxidase of the respiratory chain in long slender bloodstream forms of African trypanosomes. TAO is a cytochrome-independent, cyanide-insensitive quinol oxidase. These characteristics are distinct from those of the bacterial quinol oxidases, proteins that belong to the heme-copper terminal oxidase superfamily. The inability to purify stable TAO has severely hampered biochem. studies of the alternative oxidase family. In the present study, we were able to purify recombinant TAO to homogeneity from Escherichia coli membranes using the detergent digitonin. Kinetic anal. of the purified TAO revealed that the specific inhibitor ascofuranone is a competitive inhibitor of ubiquinol oxidase activity.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:455276 CAPLUS Full-text
DOCUMENT NUMBER: 138:49228
TITLE: Target molecule of the novel anti-Trypanosoma drug ascofuranone: trypanosome alternative oxidase
AUTHOR(S): Nihei, Koichi; Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medicine, University of Tokyo, Japan
SOURCE: Kagaku to Kyoiku (2002), 50(5), 350-354
CODEN: KAKYEY; ISSN: 0386-2151
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, discussing the action mechanism and pharmacol. of the anti-Trypanosoma drug ascofuranone against Trypanosoma brucei infestation by targeting trypanosome alternative oxidase.

L45 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:279181 CAPLUS Full-text
DOCUMENT NUMBER: 139:97132
TITLE: Purification of recombinant trypanosome alternative oxidase
AUTHOR(S): Kawai, K.; Nihei, C.; Fukai, Y.; Yabu, Y.; Ohta, N.; Minagawa, N.; Nagai, K.; Kita, K.
CORPORATE SOURCE: Department of Biomedical Chemistry, Graduate School of Medicine, The University of Tokyo, Japan
SOURCE: Parasitology--ICOPA X: Symposia, Workshops and Contributed Papers, Proceedings of the International Congress, 10th, Vancouver, BC, Canada, Aug. 4-9, 2002 (2002), 295-301. Monduzzi Editore: Bologna, Italy. CODEN: 69DTB8; ISBN: 88-323-2804-6
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Trypanosome alternative oxidase (TAO) is the terminal oxidase of the respiratory chain of long slender bloodstream forms (LS forms) of African trypanosome, which causes sleeping sickness in human and nagana in cattle. TAO is a cytochrome-independent, cyanide-insensitive quinol oxidase and these properties are quite different from those of the bacterial quinol oxidase which belongs to the heme-copper terminal oxidase superfamily. Only little information concerning the mol. structure and enzymic features of TAO have been available, whereas the bacterial enzyme has been well characterized. In the present study, we constructed an E. coli expression system for TAO. The recombinant TAO (rTAO) was expressed in E. coli ΔhemA mutant, FN 102/pTAO and purified from the membrane of the E. coli to homogeneity.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:476087 CAPLUS Full-text
DOCUMENT NUMBER: 138:82708
TITLE: Trypanosome alternative oxidase as a target of chemotherapy
AUTHOR(S): Nihei, Coichi; Fukai, Yoshihisa; Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medicine, Department of Biomedical Chemistry, University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Biochimica et Biophysica Acta, Molecular Basis of Disease (2002), 1587(2-3), 234-239 CODEN: BBADEX; ISSN: 0925-4439
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Parasites have developed a variety of physiol. functions necessary for their survival within the specialized environment of the host. Using metabolic systems that are very different from those of the host, they can adapt to low oxygen tension present within the host animals. Most parasites do not use the oxygen available within the host to generate ATP, but rather employ systems anaerobic metabolic pathways. The enzymes in these parasite-specific pathways are potential targets for chemotherapy. Cyanide-insensitive trypanosome alternative oxidase (TAO) is the terminal oxidase of the respiratory chain of long slender bloodstream forms of the African trypanosome, which causes sleeping sickness in human and nagana in cattle. TAO has been targeted for the development of anti-trypanosomal drugs because it does not exist in the host. Recently, we found the most potent inhibitor

of TAO to date, ascofuranone, a compound isolated from the phytopathogenic fungus, Ascochyta visiae.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:511240 CAPLUS Full-text
DOCUMENT NUMBER: 138:1625
TITLE: Strain-specific difference in amino acid sequences of trypanosome alternative oxidase
AUTHOR(S): Fukai, Yoshihisa; Nihei, Coichi; Yabu, Yoshisada; Suzuki, Takasi; Ohta, Nobuo; Minagawa, Nobuko; Nagai, Kazuo; Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medicine, Department of Biomedical Chemistry, The University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Parasitology International (2002), 51(2), 195-199
CODEN: PAINFD; ISSN: 1383-5769
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyanide-insensitive trypanosome alternative oxidase (TAO) is the terminal oxidase of the respiratory chain of long slender bloodstream forms of the African trypanosome, which causes sleeping sickness in human and nagana in cattle. TAO has been targeted for the development of anti-trypanosomal drugs because it does not exist in the host. The cDNA for TAO has been cloned from Trypanosoma brucei brucei EATRO110 strain and has been used for further characterization. In this study, we found amino acid sequence of the C-terminal part of TAO from the strain that we are using, T. b. brucei TC221, is considerably different from that of the EATRO110 strain.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:509982 CAPLUS Full-text
DOCUMENT NUMBER: 137:290812
TITLE: Characterization of the dihydroorotate dehydrogenase as a soluble fumarate reductase in Trypanosoma cruzi
AUTHOR(S): Takashima, Eizo; Inaoka, Daniel Ken; Osanai, Arihiro; Nara, Takeshi; Odaka, Masao; Aoki, Takashi; Inaka, Kozi; Harada, Shigeharu; Kita, Kiyoshi
CORPORATE SOURCE: Department of Biomedical Chemistry, The University of Tokyo, Graduate School of Medicine, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Molecular and Biochemical Parasitology (2002), 122(2), 189-200
CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trypanosoma cruzi, a protozoan causing Chagas' disease, excretes a considerable amount of succinate even though it uses the TCA cycle and the aerobic respiratory chain. For this reason, it was believed that unknown metabolic pathways participate in succinate production in this parasite. In the present study, we examined the mol. properties of dihydroorotate dehydrogenase (DHOD), the fourth enzyme of de novo pyrimidine biosynthetic pathway, as a soluble fumarate reductase (FRD) because our sequence anal. of pyr genes cluster showed that the amino acid sequence of T. cruzi DHOD is quite similar to that of type 1A DHOD of Saccharomyces cerevisiae, an enzyme that uses fumarate as an electron acceptor and produces succinate. Biochem.

analyses of the cytosolic enzyme purified from the parasite and of the recombinant enzyme revealed that T. cruzi DHOD has methylviologen-fumarate reductase (MV-FRD) activity. In addition, T. cruzi DHOD was found to catalyze electron transfer from dihydroorotate to fumarate by a ping-pong Bi-Bi mechanism. The recombinant enzyme contained FMN as a prosthetic group. Dynamic light scattering anal. indicated that T. cruzi DHOD is a homodimer. These results clearly indicated that the cytosolic MV-FRD is attributable to T. cruzi DHOD. The DHOD may play an important role in succinate/fumarate metabolism as well as de novo pyrimidine biosynthesis in T. cruzi.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:103671 CAPLUS Full-text
DOCUMENT NUMBER: 136:98883
TITLE: Adaptation to low oxygen tension in parasite mitochondria
AUTHOR(S): Kita, Kiyoshi
CORPORATE SOURCE: Grad. Sch. Med., The Univ. Tokyo, Japan
SOURCE: Tanpakushitsu Kakusan Koso (2002), 47(1), 37-44
CODEN: TAKKAJ; ISSN: 0039-9450
PUBLISHER: Kyoritsu Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on the functions of mitochondria of protozoa, changes of mitochondrial functions of Trypanosome brucei brucei during life cycle, structure and function of trypanosome alternative oxidase (cyanide-insensitive quinol oxidase), inhibition of glycerol-3-phosphate- dependent mitochondrial O2 consumption by antitrypanosome drug ascofuranone, changes of energy metabolism and respiratory chain in Ascaris suum in response to oxygen tension during life-cycle, NADH-fumarate reductase system of adult A. suum, functions of complex II as a succinate-ubiquinone reductase in larvae and as a quinol-fumarate reductase in adults, association of mitochondrial quinol-fumarate reductase activity with parasitic adaptation, evolution of quinones, and importance of the parasite mitochondrias as targets of chemotherapeutic agents against parasites.

L45 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:350991 CAPLUS Full-text
DOCUMENT NUMBER: 135:163655
TITLE: environmental adaptation of the respiratory system in parasites
AUTHOR(S): Kita, Kiyoshi
CORPORATE SOURCE: Graduate School of Medical Research, University of Tokyo, Japan
SOURCE: Shirizu Baiosaiensu no Shinseiki (2000), Volume 7, 47-59. Editor(s): Yoshida, Masasuke; Mogi, Tatsushi. Kyoritsu Shuppan: Tokyo, Japan.
CODEN: 69BHTE
DOCUMENT TYPE: Conference; General Review
LANGUAGE: Japanese

AB A review with 20 refs., on changes of mitochondrial respiratory chains in parasites (such as Ascaris suum and Trypanosoma brucei brucei) and their relations to the parasitic life cycle and environmental adaptation.

L45 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:686146 CAPLUS Full-text
DOCUMENT NUMBER: 132:60821

TITLE: Functional expression of the ascofuranone-sensitive Trypanosoma brucei brucei alternative oxidase in the cytoplasmic membrane of Escherichia coli
AUTHOR(S): Fukai, Y.; Amino, H.; Hirawake, H.; Yabu, Y.; Ohta, N.; Minagawa, N.; Sakajo, S.; Yoshimoto, A.; Nagai, K.; Takamiya, S.; Kojima, S.; Kita, K.
CORPORATE SOURCE: Bunkyo-ku, 7-3-1 Hongo, Graduate School of Medicine, Department of Biomedical Chemistry, The University of Tokyo, Tokyo, Japan
SOURCE: Comparative Biochemistry and Physiology, Part C: Pharmacology, Toxicology & Endocrinology (1999), 124C(2), 141-148
CODEN: CBPCEE; ISSN: 0742-8413
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Trypanosoma alternative oxidase (TAO) is the terminal oxidase of the respiratory chain of long slender bloodstream forms (LS forms) of African trypanosoma, which causes sleeping sickness in human and nagana in cattle. TAO is a cytochrome-independent, cyanide-insensitive quinol oxidase and these properties are quite different from those of the bacterial quinol oxidase which belongs to the heme-copper terminal oxidase superfamily. Only little information concerning the mol. structure and enzymic features of TAO have been available, whereas the bacterial enzyme has been well characterized. In this study, a cDNA encoding TAO from Trypanosoma brucei brucei was cloned into the expression vector pET15b (pTAO) and recombinant TAO was expressed in Escherichia coli. The growth of the transformant carrying pTAO was cyanide-resistant. A peptide with a mol. mass of 37 kDa was found in the cytoplasmic membrane of E. coli, and was recognized by antibodies against plant-type alternative oxidases from Sauromatum guttatum and Hansenula anomala. Both the ubiquinol oxidase and succinate oxidase activities found in the membrane of the transformant were insensitive to cyanide, while those of the control strain, which contained vector alone, were inhibited. This cyanide-insensitive growth of the E. coli carrying pTAO was inhibited by the addition of ascofuranone, a potent and specific inhibitor of TAO ubiquinol oxidase. The ubiquinol oxidase activity of the membrane from the transformant was sensitive to ascofuranone. These results clearly show the functional expression of TAO in E. coli and indicate that ubiquinol-8 in the E. coli membrane is able to serve as an electron donor to the recombinant enzyme and confer cyanide-resistant and ascofuranone-sensitive growth to E. coli. This system will facilitate the biochem. characterization of the novel terminal oxidase, TAO, and the understanding on the mechanism of the trypanocidal effect of ascofuranone.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:400327 CAPLUS Full-text
DOCUMENT NUMBER: 129:117469
TITLE: Trypanocidal effects of curcumin in vitro
AUTHOR(S): Nose, Mitsuhiko; Koide, Tatsuo; Ogihara, Yukio; Yabu, Yoshisada; Ohta, Nobuo
CORPORATE SOURCE: Department of Pharmacognosy and Plant Chemistry, Faculty of Pharmaceutical Sciences, Nagoya City University, Nagoya, 467, Japan
SOURCE: Biological & Pharmaceutical Bulletin (1998), 21(6), 643-645
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Searching for antiparasitic agents from natural sources revealed that curcumin is cytotoxic against African trypanosomes in vitro. The LD50 values of curcumin were 4.77±0.91 μM for blood stream forms and 46.52±4.94 μM for procyclic forms of Trypanosoma brucei brucei (GUTat 3.1 clone).
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:400313 CAPLUS Full-text
DOCUMENT NUMBER: 129:132403
TITLE: Formation of reactive oxygen intermediates might be involved in the trypanocidal activity of gallic acid
AUTHOR(S): Nose, Mitsuhiko; Koide, Tatsuo; Morikawa, Kyoko; Inoue, Makoto; Ogihara, Yukio; Yabu, Yoshisada; Ohta, Nobuo
CORPORATE SOURCE: Department of Pharmacognosy and Plant Chemistry, Faculty of Pharmaceutical Sciences, Nagoya City University, Nagoya, 467, Japan
SOURCE: Biological & Pharmaceutical Bulletin (1998), 21(6), 583-587
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors investigated the mechanism of the trypanocidal activity of gallic acid (GA). GA-induced trypanocidal activity was significantly reduced by pretreatment with superoxide dismutase (SOD) and/or catalase. The ESR technique with 5,5-dimethyl-1-pyrroline N-oxide (DMPO) as a spin trapping agent revealed that a DMPO-OH adduct was detected in culture medium containing GA. The intensity of ESR signals of the DMPO-OH adduct was increased in a time dependent manner. SOD also inhibited the formation of GA-induced DMPO-OH adducts. Furthermore, GA enhanced DNA single-strand breaks induced by Fenton reagent. These results suggest the possibility that GA acts as a pro-oxidant for trypanocidal activity.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:26547 CAPLUS Full-text
DOCUMENT NUMBER: 130:265982
TITLE: Parasite infection and apoptosis
AUTHOR(S): Kita, Kiyoshi; Shimada, Junko
CORPORATE SOURCE: Graduate School of Medicine, The University of Tokyo, Japan
SOURCE: Igaku no Ayumi (1998), 187(5), 436-440
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 19 refs., on apoptosis of parasite-infected host cells; infection by Leishmania, Toxoplasma, and Trypanosoma; malaria or Trypanosoma infection-induced apoptosis of host immunocytes, and apoptosis of parasite.

L45 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:522580 CAPLUS Full-text
DOCUMENT NUMBER: 129:270006
TITLE: Oral and intraperitoneal treatment of Trypanosoma brucei brucei with a combination of ascofuranone and

glycerol in mice
AUTHOR(S): Yabu, Yoshisada; Minagawa, Nobuko; Kita, Kiyoshi; Nagai, Kazuo; Honma, Masakatsu; Sakajo, Shigeru; Koide, Tatsuo; Ohta, Nobuo; Yoshimoto, Akio
CORPORATE SOURCE: Department of Medical Zoology, Medical School, Nagoya City University, Nagoya, 467-8601, Japan
SOURCE: Parasitology International (1998), 47(2), 131-137
CODEN: PAINFD; ISSN: 1383-5769
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A suspension of ascofuranone (6-200 mg/kg) was given orally or i.p., and then glycerol (1 g/kg) was administered orally or i.p. at 30-min intervals to mice heavily parasitemic with T. brucei brucei. Both orally (100 mg/kg) and i.p. (25 mg/kg) administered ascofuranone, combined with a total dose of 3 g glycerol/kg, produced potent antitrypanosomal activity in infested mice. The trypanocidal activity of ascofuranone was very powerful, and all trypanosomes had disappeared within 30 and 180 min after final i.p. and oral treatment, resp. This combination treatment showed high efficacy and low toxicity. Ascofuranone in combination with glycerol may be an effective tool in chemotherapy for African trypanosomiasis.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:98846 CAPLUS Full-text
DOCUMENT NUMBER: 128:149258
TITLE: Trypanocidal effects of gallic acid and related compounds
AUTHOR(S): Koide, Tatsuo; Nose, Mitsuhiko; Inoue, Makoto; Ogihara, Yukio; Yabu, Yoshisada; Ohta, Nobuo
CORPORATE SOURCE: Dep. Pharmacognosy Plant Chemistry, Fac. Pharmaceutical Sciences, Nagoya City Univ., Nagoya, 467, Japan
SOURCE: Planta Medica (1998), 64(1), 27-30
CODEN: PLMEAA; ISSN: 0032-0943
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gallic acid (3,4,5-trihydroxybenzoic acid) is a naturally abundant plant phenolic compound and it is well known as a component of hydrolyzable tannins. We report here that gallic acid and related compds. have trypanocidal activity against Trypanosoma brucei brucei (GUTat 3.1) in both the long slender bloodstream forms and the procyclic forms, in vitro. LD50 values of gallic acid are 46.96 ± 1.28 μM for bloodstream forms and 30.02 ± 3.49 for procyclic forms, resp. A study of structurally related compds. suggested that the pyrogallol moiety could be responsible for this activity.

L45 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:179701 CAPLUS Full-text
DOCUMENT NUMBER: 126:180891
TITLE: An antibiotic, ascofuranone, specifically inhibits respiration and in vitro growth of long slender bloodstream forms of trypanosoma brucei brucei. [Erratum to document cited in CA125:265065]
AUTHOR(S): Minagawa, Nobuko; Yabu, Yoshisada; Kita, Kiyoshi; Nagai, Kazuo; Ohta, Nobuo; Meguro, Keiichi; Sakajo, Shigeru; Yoshimoto, Akio
CORPORATE SOURCE: Department of Biochemistry, Niigata College of

Pharmacy, Niigata, 950-21, Japan
SOURCE: Molecular and Biochemical Parasitology (1997), 84(2), 271-280
CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstract or the index entries.

L45 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:583098 CAPLUS Full-text
DOCUMENT NUMBER: 125:265065
TITLE: An antibiotic, ascofuranone, specifically inhibits respiration and in vitro growth of long slender bloodstream forms of Trypanosoma brucei brucei
AUTHOR(S): Minagawa, Nobuko; Yabu, Yoshisada; Kita, Kiyoshi; Nagai, Kazuo; Ohta, Nobuo; Meguro, Keiichi; Sakajo, Shigeru; Yoshimoto, Akio
CORPORATE SOURCE: Department of Biochemistry, Niigata College of Pharmacy, 5-13-2 Kamishin'ei-cho, Niigata, 950-21, Japan
SOURCE: Molecular and Biochemical Parasitology (1996), 81(2), 127-136
CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ascofuranone, a prenylphenol antibiotic isolated from a phytopathogenic fungus, Ascochyta visiae, strongly inhibited both glucose-dependent cellular respiration and glycerol-3-phosphate-dependent mitochondrial O2 consumption of long slender bloodstream forms of Trypanosoma brucei brucei. This inhibition was suggested to be due to inhibition of the mitochondrial electron-transport system, composed of glycerol-3-phosphate dehydrogenase (EC 1.1.99.5) and plant-like alternative oxidase. Ascofuranone noncompetitively inhibited the reduced coenzyme Q1-dependent O2 uptake of the mitochondria with respect to ubiquinol (Ki = 2.38 nM). Therefore, the susceptible site is deduced to be the ubiquinone redox machinery which links the two enzyme activities. Further, ascofuranone in combination with glycerol completely blocked energy production, and potently inhibited the in vitro growth of the parasite. Our findings suggest that ascofuranone might be a promising candidate for the chemotherapeutic agents of African trypanosomiasis.

L45 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:78987 CAPLUS Full-text
DOCUMENT NUMBER: 118:78987
TITLE: Inhibition of IgM antibody-mediated aggregation of Trypanosoma gambiense in the presence of complement
AUTHOR(S): Takayanagi, T.; Kawaguchi, H.; Yabu, Y.; Itoh, M.; Yano, K.
CORPORATE SOURCE: Med. Sch., Nagoya City Univ., Nagoya, 467, Japan
SOURCE: Experientia (1992), 48(10), 1002-6
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The immune reaction was studied between T. gambiense and monoclonal IgM mouse antibody at equivalence with or without rabbit complement. Antibody-mediated trypanosome clumps formed in the absence of complement, and were readily dissociated by complement to become free. In the presence of complement, on

the other hand, T. gambiense was not aggregated by the antibody. Free parasites adhered readily to cultured peritoneal macrophages. Complement-mediated dissociation of the clumped trypanosomes in the equivalence area released a large number of previously bound surface antigens. These antigens were capable of binding again to fresh IgM antibody. The complement system caused a functional alternation, changing the multivalent nature of the IgM antibody in the immune complex into a univalent one. This phenomenon is of great advantage to the infected host in clearing pathogens in vivo, as it allows more antibodies to attach to trypanosomes and subsequently initiate complement activity.

L45 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:513991 CAPLUS Full-text
DOCUMENT NUMBER: 107:113991
TITLE: Contribution of the complement system to antibody-mediated binding to Trypanosoma gambiense to macrophages
AUTHOR(S): Takayanagi, Tan; Kawaguchi, Hitoshi; Yabu, Yoshisada; Ito, Makoto; Appawu, Maxwell Alex
CORPORATE SOURCE: Med. Sch., Nagoya City Univ., Nagoya, 467, Japan
SOURCE: Journal of Parasitology (1987), 73(2), 333-41
CODEN: JOPAA2; ISSN: 0022-3395
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of complement in the process of binding of trypanosomes to macrophages in the presence of specific antibody was studied. The aggregation of trypanosomes observed at the optimal antigen-antibody ratio or in the presence of excess antigen inhibited the binding. Complement caused clumped trypanosomes to dissociate, and the free trypanosomes, which were presumed to be coated with antibody that had fixed complement, readily attached to surfaces of phagocytes. Thus, complement contributed at the site of the antigen-antibody reaction to the creation of an environment suitable for the binding. Apparently, the trypanosomes dissociated by complement adhered to C3 receptors of the macrophage. However, in the absence of complement and in regions of antibody excess, free trypanosomes also attached to phagocytes. Thus, phagocytes may also have receptors for the Fc portion of aggregated antibody. Complement activated by the alternate pathway also enhanced attachment of trypanosomes to phagocytes, but the effect was not as rapid as it was when complement was activated by classical means.

L45 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:421830 CAPLUS Full-text
DOCUMENT NUMBER: 97:21830
ORIGINAL REFERENCE NO.: 97:3821a,3824a
TITLE: A monoclonal antibody defining antigenic determinants on subpopulations of mammalian neurons and Trypanosoma cruzi parasites
AUTHOR(S): Wood, J. N.; Hudson, L.; Jessell, T. M.; Yamamoto, M.
CORPORATE SOURCE: Dep. Immunol., St. George'S Hosp. Med. Sch., London, SW17 0RE, UK
SOURCE: Nature (London, United Kingdom) (1982), 296(5852), 34-8
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An IgM λ class monoclonal antibody was raised against membranes from rat dorsal root ganglia; it defined a novel antigenic determinant expressed by subpopulations of mammalian central and peripheral neurons. In the presence of

complement it was cytotoxic to mammalian neurons in vitro. The same antibody also labeled T. cruzi, the protozoan responsible for Chagas' disease. Neurons labeled by the antibody were those that degenerate during this disease; thus, the labeled antigens, common to neuron and parasite, may be important in the pathogenesis of the disease.

L45 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:120651 CAPLUS Full-text
DOCUMENT NUMBER: 96:120651
ORIGINAL REFERENCE NO.: 96:19791a,19794a
TITLE: Lectin binding sites of Trypanosoma gambiense
AUTHOR(S): Yabu, Yoshisada
CORPORATE SOURCE: Med. Sch., Nagoya City Univ., Nagoya, 467, Japan
SOURCE: Nagoya Medical Journal (1981), 26(1-2), 35-52
CODEN: NMJOAA; ISSN: 0027-7649
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intact T. gambiense was not agglutinated by Con A, wheat germ agglutinin (WGA), soybean agglutinin (SBA), phytohemagglutinins M and P, Ricinus communis agglutinin-I, and peanut agglutinin. However, the parasites were agglutinated specifically by low concns. of these lectins after treatment by trypsin, chymotrypsin, papain, chymopapain, or pronase. Ulex europaeus Agglutinin-I and Dolichos biflorus agglutinin did not induce the agglutination of either the intact or enzyme-treated parasites. Dextranase and α-amylase treatment of the protease-digested parasites did not reduce agglutination by lectins. Agglutination with lectins did not occur when an inhibitory concentration of a competitive sugar was present. Lectin-binding sites on the cell surface of T. gambiense were not directly associated with α-1,4 or α-1,6 glycosidic bonds of polysaccharides. Con A sites on the cell surface were visualized at the fine structure level with a lectin-ferritin conjugate. The electron-dense ferritin particles were distributed randomly on the enzyme-treated cell surface and flagella membrane. Con A bound at the cell surface was also visualized with horseradish peroxidase (HRP) and diaminobenzidine (DAB)-coupled reactions. A dense Con A-HRP-DAB reaction product was deposited uniformly over the entire cell surface and flagella membrane. Localization of WGA and SBA bound at the T. gambiense cell surface was also facilitated using HRP-DAB-coupled reactions. The fine structure distribution of these HRP-conjugated lectins was similar to that obtained with Con A-HRP-DAB prepns. Both the living and glutaraldehyde-fixed parasites gave similar agglutination results with Con A. The parasites also showed strong agglutination by Con A at low temperature Colchicine- and cytochalasin B-pretreated parasites also showed marked agglutination by Con A. Thus, parasite agglutination by Con A differs from mammalian cell agglutination, since clustering of Con A-binding sites is not necessary for parasite agglutination.

L45 ANSWER 41 OF 42 CONFSCI COPYRIGHT 2008 CSA on STN
ACCESSION NUMBER: 2007:92194 CONFSCI
DOCUMENT NUMBER: 07-064010
TITLE: Structural Insights into Mechanisms of Dihydroorotate Oxidation and Fumarate Reduction Catalyzed by Trypanosoma cruzi Dihydroorotate Dehydrogenase.
AUTHOR: Inaoka, D. K.; Sakamoto, K.; Shimizu, H.; Shiba, T.; Kurisu, G.; Nara, T.; Aoki, T.; Kita, K.; Harada, S.
CORPORATE SOURCE: The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan.
SOURCE: 000 0000: 2nd International Symposium on Diffraction Structural Biology (ISDSB 2007) (0000000). Tower Hall Funabori, Tokyo (Japan). 10-13 Sep 2007. Professor Takashi

Yamane.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: UNAVAILABLE

L45 ANSWER 42 OF 42 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-333264 [34] WPIX
CROSS REFERENCE: 2005-333263
DOC. NO. CPI: C2005-103571 [34]
TITLE: Novel phenol derivatives, useful as antitrypanosoma agent for preventing and treating disease e.g. trypanosomiasis caused by trypanosoma
DERWENT CLASS: B05
INVENTOR: HOSOKAWA T; KITA K ; SAIMOTO H; SHIGEMASA Y; YABU Y; YAMAMOTO M; TOMOYOSHI H
PATENT ASSIGNEE: (ARIG-N) ARIGEN INC
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005037760	A1	20050428	(200534)*	JA	73[0]	
EP 1681280	A1	20060719	(200647)	EN		
AU 2004282055	A1	20050428	(200680)	EN		
JP 2005514824	X	20061228	(200702)	JA	62	
KR 2006097731	A	20060914	(200705)	KO		
US 20070208078	A1	20070906	(200759)	EN		
IN 2006DN02774	P1	20070803	(200771)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005037760	A1	WO 2004-JP15390	20041018
AU 2004282055	A1	AU 2004-282055	20041018
EP 1681280	A1	EP 2004-792559	20041018
EP 1681280	A1	WO 2004-JP15390	20041018
JP 2005514824	X	WO 2004-JP15390	20041018
KR 2006097731	A	WO 2004-JP15390	20041018
US 20070208078	A1	WO 2004-JP15390	20041018
JP 2005514824	X	JP 2005-514824	20041018
KR 2006097731	A	KR 2006-709515	20060516
US 20070208078	A1	US 2006-575653	20061213
IN 2006DN02774	P1	WO 2004-JP15390	20041018
IN 2006DN02774	P1	IN 2006-DN2774	20060517

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1681280	A1	Based on	WO 2005037760	A
AU 2004282055	A1	Based on	WO 2005037760	A
JP 2005514824	X	Based on	WO 2005037760	A
KR 2006097731	A	Based on	WO 2005037760	A

PRIORITY APPLN. INFO: WO 2003-JP13310 20031017
AN 2005-333264 [34] WPIX
CR 2005-333263
AB WO 2005037760 A1 UPAB: 20051222

NOVELTY - Phenol derivatives (I) are new.

DETAILED DESCRIPTION - Phenol derivatives of formula (I) and their salts and optical isomers are new.

X = H or halogen;

R1 = H or -(CnH2n)-R';

n = 1-5;

R' = COOR'' (substituted by H or n carbon atoms);

R'' = H, 1-4C alkyl or -COR''';

R''' = pyridyl group, amino (substituted by 1-4C alkyl), phenoxyalkyl (substituted by halogen on alkyl chain or benzene ring) or phenyl group (substituted by 1-4C alkoxy or 1-4C alkoxycarbonyl group);

R2 = H or 1-4C alkyl;

R3 = -CHO or -COOH;

R4 = -CH=CH-(CH2)p-CH3, -CH-(OH)-(CH2)q-CH3, -CH(OH)-CH2-CH(CH3)-(CH2)2-CH=C(CH3)2, -CH=CH-CH(CH3)-(CH2)3-CH(CH3)2, -(CH2)2-CH(CH3)-(CH2)3-CH(CH3)2 or -(CH2)8-CH3;

p = 1-12; and

q = 1-13.

INDEPENDENT CLAIMS are included for the following:

(1) composition which contains (I);

(2) antitrypanosoma agent which contains (I);

(3) manufacture of antitrypanosoma agent; and

(4) use of antitrypanosoma agent.

ACTIVITY - Protozoacide.

Antitrypanosoma effect of 3-chloro-4,6-dihydro-2-methyl-5-(3- methyl-7-(tetrahydro-5,5-dimethyl-4-oxo-2-furanyl)octyl)benzaldehdye (Ia) with respect to cyanogen resistant quinol enzyme of trypanosoma was evaluated using recombinant enzyme. (Ia) showed IC50 of 0.3 mM.

MECHANISM OF ACTION - None given.

USE - As antitrypanosoma agent for preventing and treating disease (claimed) e.g. trypanosomiasis caused by trypanosoma.

ADVANTAGE - (I) has trypanosomiasis inhibitory effect higher than ascofuranone at low concentration.

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=> d his nofile

     (FILE 'HOME' ENTERED AT 11:10:38 ON 20 FEB 2008)

     FILE 'REGISTRY' ENTERED AT 11:10:44 ON 20 FEB 2008
L1             STR
L2           0 SEA SSS SAM L1
L3          20 SEA SSS FUL L1
L4             STR
L5           3 SEA SSS SAM L4
L6          46 SEA SSS FUL L4

     FILE 'CAPLUS' ENTERED AT 11:39:00 ON 20 FEB 2008
L7           1 SEA ABB=ON  PLU=ON  L3
L8          96 SEA ABB=ON  PLU=ON  L6

     FILE 'REGISTRY' ENTERED AT 11:39:18 ON 20 FEB 2008
L9             STR L4
L10          2 SEA SUB=L6 SSS SAM L9
L11         32 SEA SUB=L6 SSS FUL L9

     FILE 'CAPLUS' ENTERED AT 11:42:36 ON 20 FEB 2008
L12         93 SEA ABB=ON  PLU=ON  L11
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L13             ANALYZE PLU=ON  L12 1-93 RN :    1785 TERMS
                D

     FILE 'REGISTRY' ENTERED AT 11:43:04 ON 20 FEB 2008
L14           1 SEA ABB=ON  PLU=ON  38462-04-3
                D
L15          31 SEA ABB=ON  PLU=ON  L11 NOT L14

     FILE 'CAPLUS' ENTERED AT 11:44:59 ON 20 FEB 2008
L16          34 SEA ABB=ON  PLU=ON  L15

     FILE 'REGISTRY' ENTERED AT 11:45:09 ON 20 FEB 2008
L17           0 SEA ABB=ON  PLU=ON  L15 AND C18H25CLO4/MF
L18           5 SEA ABB=ON  PLU=ON  L15 AND C=18
                D SCA
L19           2 SEA ABB=ON  PLU=ON  L18 AND H=25
                D SCA
L20           1 SEA ABB=ON  PLU=ON  L18 AND H=27
                D SCA
L21           0 SEA ABB=ON  PLU=ON  L11 AND C=21
L22          15 SEA ABB=ON  PLU=ON  L11 AND OC4/ES
L23          15 SEA ABB=ON  PLU=ON  L22 AND O=5
L24           0 SEA ABB=ON  PLU=ON  L23 AND N=1
L25           0 SEA ABB=ON  PLU=ON  H=23 AND L23
L26           3 SEA ABB=ON  PLU=ON  H=33 AND L23
L27           3 SEA ABB=ON  PLU=ON  H=31 AND L23
                D SCA L26
L28           0 SEA ABB=ON  PLU=ON  L26 AND C=23
L29           3 SEA ABB=ON  PLU=ON  L11 AND C=24
                D SCA
                E BENZALDEHYDE, 3-CHLORO-6-HYDROXY-4-METHOXY-2-METHYL-5-((2E,6E
L30           1 SEA ABB=ON  PLU=ON  "BENZALDEHYDE, 3-CHLORO-6-HYDROXY-4-METHOXY
                -2-METHYL-5-((2E,6E)-3-METHYL-7-((2S)-TETRAHYDRO-5,5-DIMETHYL-4
                -OXO-2-FURANYL)-2,6-OCTADIENYL)-"/CN
                D SCA
                D
L31          21 SEA ABB=ON  PLU=ON  L3 OR L30

     FILE 'CAPLUS' ENTERED AT 12:03:19 ON 20 FEB 2008
L32           3 SEA ABB=ON  PLU=ON  L31

     FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 12:05:30 ON 20 FEB 2008
                E SAIMOTO H/AU
L33         206 SEA ABB=ON  PLU=ON  ("SAIMOTO H"/AU OR "SAIMOTO HIROYUKI"/AU
                OR "SAIMOTO HIRYUKI"/AU)
                E SHIGEMASA Y/AU
L34         286 SEA ABB=ON  PLU=ON  ("SHIGEMASA Y"/AU OR "SHIGEMASA YOSHIHIRO"/
                AU OR "SHIGEMASA YOSHIHRO"/AU)
                E KITA K/AU
L35        1742 SEA ABB=ON  PLU=ON  ("KITA K"/AU OR "KITA K A"/AU OR "KITA K
                F"/AU OR "KITA K K F S P"/AU OR "KITA K M B"/AU OR "KITA K M
                C"/AU OR "KITA K N G K K K K"/AU OR "KITA K S C"/AU OR "KITA
                KIYOSHI"/AU)
                E YOSHISADA Y/AU
                E YABU Y/AU
L36          85 SEA ABB=ON  PLU=ON  ("YABU Y"/AU OR "YABU Y T"/AU OR "YABU
                YOSHISADA"/AU)
                E HOSOKAWA T/AU
L37        1970 SEA ABB=ON  PLU=ON  ("HOSOKAWA TOMOYOSHI"/AU OR "HOSOKAWA
                T"/AU OR "HOSOKAWA T C O F"/AU OR "HOSOKAWA T D C"/AU OR
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                "HOSOKAWA T F I C L"/AU OR "HOSOKAWA T I G C L"/AU OR "HOSOKAWA
                 T L"/AU OR "HOSOKAWA T N D C"/AU OR "HOSOKAWA T T G C L"/AU
                OR "HOSOKAWA T Y F L"/AU)
                E YAMAMOTO M/AU
L38         17371 SEA ABB=ON  PLU=ON  ("YAMAMOTO MASAICHI"/AU OR "YAMAMOTO M"/AU
                OR "YAMAMOTO M 0"/AU OR "YAMAMOTO M A"/AU OR "YAMAMOTO M B"/AU
                OR "YAMAMOTO M B K K K"/AU OR "YAMAMOTO M C"/AU OR "YAMAMOTO M
                C O M"/AU OR "YAMAMOTO M D"/AU OR "YAMAMOTO M D I L"/AU OR
                "YAMAMOTO M D K K"/AU OR "YAMAMOTO M D M"/AU OR "YAMAMOTO M D
                M C L"/AU OR "YAMAMOTO M D N P C L"/AU OR "YAMAMOTO M D P C C
                L"/AU OR "YAMAMOTO M D R L"/AU OR "YAMAMOTO M E"/AU OR
                "YAMAMOTO M E C"/AU OR "YAMAMOTO M E I"/AU OR "YAMAMOTO M
                EMILIA"/AU OR "YAMAMOTO M F"/AU OR "YAMAMOTO M F L"/AU OR
                "YAMAMOTO M F P F C L"/AU OR "YAMAMOTO M G C"/AU OR "YAMAMOTO
                M H I"/AU OR "YAMAMOTO M H L"/AU OR "YAMAMOTO M H M C L"/AU OR
                "YAMAMOTO M I"/AU OR "YAMAMOTO M I F D K K"/AU OR "YAMAMOTO M
                I P D N D I"/AU OR "YAMAMOTO M J"/AU OR "YAMAMOTO M J L"/AU OR
                "YAMAMOTO M K"/AU OR "YAMAMOTO M K C I C L"/AU OR "YAMAMOTO M
                K F"/AU OR "YAMAMOTO M K F S P"/AU OR "YAMAMOTO M K S S"/AU OR
                "YAMAMOTO M L"/AU OR "YAMAMOTO M M"/AU OR "YAMAMOTO M M C"/AU
                OR "YAMAMOTO M M C C"/AU OR "YAMAMOTO M M D K K"/AU OR
                "YAMAMOTO M M E W L"/AU OR "YAMAMOTO M M H I L"/AU OR "YAMAMOTO
                 M M M"/AU OR "YAMAMOTO M M S K L"/AU OR "YAMAMOTO M M S K L P
                R C"/AU OR "YAMAMOTO M N"/AU OR "YAMAMOTO M N C I L"/AU OR
                "YAMAMOTO M N C N F"/AU OR "YAMAMOTO M N D C"/AU OR "YAMAMOTO
                M N D I"/AU OR "YAMAMOTO M N P C L"/AU OR "YAMAMOTO M O P C
                L"/AU OR "YAMAMOTO M O T"/AU OR "YAMAMOTO M P"/AU OR "YAMAMOTO
                M P I C L"/AU OR "YAMAMOTO M P R C"/AU OR "YAMAMOTO M P R C
                M"/AU OR "YAMAMOTO M R L"/AU OR "YAMAMOTO M S"/AU OR "YAMAMOTO
                M S C"/AU OR "YAMAMOTO M S E I L"/AU OR "YAMAMOTO M S K C
                L"/AU OR "YAMAMOTO M S L"/AU OR "YAMAMOTO M S L O G L"/AU OR
                "YAMAMOTO M S M I L"/AU OR "YAMAMOTO M S P C L"/AU OR "YAMAMOTO
                 M S S C C L"/AU OR "YAMAMOTO M T"/AU OR "YAMAMOTO M T L"/AU
                OR "YAMAMOTO M T L T K"/AU OR "YAMAMOTO M Y"/AU OR "YAMAMOTO M
                Y F C L"/AU)
L39         21463 SEA ABB=ON  PLU=ON  (L33 OR L34 OR L35 OR L36 OR L37 OR L38)
L40           286 SEA ABB=ON  PLU=ON  L39 AND PHENOL
L41             0 SEA ABB=ON  PLU=ON  L40 AND ?PANASOM?
L42             0 SEA ABB=ON  PLU=ON  L40 AND (TRYPANASOM? OR ?PANASOM? OR
                ANTITRYPANA?)

     FILE 'CAPLUS' ENTERED AT 12:10:37 ON 20 FEB 2008
                E US2006-575653/APPS
L43             1 SEA ABB=ON  PLU=ON  US2006-575653/AP
                D SCA

     FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 12:11:33 ON 20 FEB 2008
L44            46 SEA ABB=ON  PLU=ON  L39 AND (?PANOSOM? OR TRYPANOS? OR
                ANTITRYPANOS?)

     FILE 'CAPLUS' ENTERED AT 12:12:19 ON 20 FEB 2008
                D QUE L32
                D L32 IBIB ABS HITSTR TOT

     FILE 'CAPLUS, DISSABS, CONFSCI, WPIX' ENTERED AT 12:13:05 ON 20 FEB 2008
                D QUE L44
L45            42 DUP REM L44 (4 DUPLICATES REMOVED)
                      ANSWERS '1-40' FROM FILE CAPLUS
                      ANSWER '41' FROM FILE CONFSCI
                      ANSWER '42' FROM FILE WPIX
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D L45 IBIB ABS TOT